Amendments to the Claim:

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

1 (currently amended). A process for production of recombinant ~~arylsulphatase~~ arylsulfatase A (ASA) in a continuous cell culture system, the process comprising:

i) continuously culturing a mammalian cell capable of producing said arylsulfatase A in liquid medium ~~in a system comprising one or more bio-reactors~~; and

ii) concentrating, purifying and formulating the recombinant ~~rh~~ASA by a purification process comprising one or more steps of affinity chromatography and/or ion exchange chromatography,

wherein the concentration and purification process of (ii) comprises a polishing step including a passive step, wherein the arylsulfatase A passes through a cation exchange chromatography resin or membrane and/or affinity chromatography resin, and an active step, wherein the arylsulfatase A is detained within and subsequently eluted from an anion exchange membrane or resin, and wherein the cation exchange chromatography resin or membrane and the anion ~~chromatography~~ exchange membrane or resin are coupled or connected in a series,

wherein said mammalian cell comprises a nucleotide sequence which encodes a polypeptide comprising (a) SEQ ID NOs:2 or 4 or (b) a mutant sequence at least 95% identical to SEQ ID NOs:2 or 4, and wherein said polypeptide, or a post-translationally modified product thereof that is produced by said cell, has arylsulfatase A activity.

2-7 (cancelled).

8 (previously presented). A process according to claim 1, wherein the mammalian cells are of human or primate origin.

9 (previously presented). A process according to claim 1, wherein the concentration and purification process of ii)

comprises one or more steps of Expanded Bed Chromatography.

10 (cancelled).

11 (currently amended). A process according to claim 1, wherein the concentration and purification process of ii) comprises the following steps:

II) contacting an arylsulfatase A containing supernatant on an equilibrated chromatography column and eluting one or more fraction(s) containing arylsulfatase A;

III) loading the fraction(s) from step II on another equilibrated chromatography column and eluting one or more fraction(s) containing arylsulfatase A;

IV) buffer exchange of the arylsulfatase A present in the fraction(s) from step III by tangential flow filtration;

V) polishing the preparation of arylsulfatase A from step IV in one or two or more successive steps, each step comprising loading the preparation on an equilibrated chromatography columns and eluting one or more fraction(s) containing arylsulfatase A;

VI) passing the fraction(s) from step V through a viral reduction filter <u>and/or inactivating virus in said fraction(s) with a virus inactivating agent</u>;

VII) formulating the fraction(s) from step VI in order to obtain a preparation of arylsulfatase A in a suitable formulation buffer;

VIII) optionally filling the formulated preparation of arylsulfatase A into a suitable container and freeze-drying the sample.

12 (original). A process according to claim 11, further comprising an initial step I) of concentrating the arylsulfatase A by tangential flow filtration.

13 (previously presented). A process according to claim 11, wherein the chromatography column used in step II of the purification process is an anion exchange column.

14 (original). A process according to claim 13, wherein said anion exchange column is a DEAE Sepharose column or a DEAE Streamline column.

15 (previously presented). A process according to claim 11, wherein the chromatography column used in step III of the purification process is a hydrophobic interaction column.

16 (previously presented). A process according to claim 11, wherein purification of the sample in step IV of the purification process is accomplished by tangential flow filtration.

17 (cancelled).

18 (currently amended). A process according to claim 11, wherein the ~~filtration of the sample as performed in step VI of the purification process is replaced by or combined with contacting the sample with~~ inactivating agent is a detergent~~, preferably prior to step V or preferably prior to step Ii of the purification process~~.

19-41 (cancelled).

42 (new). The process of claim 1 wherein the continuous culturing is for a period of at least one week.

43 (new). The process of claim 1 wherein the arylsulfatase has a specific arylsulfatase A activity of at least 20 units/mg.

44 (new). The process of claim 1 wherein the mutant sequence is at least 96% identical to SEQ ID NO:2 or 4.

45 (new). The process of claim 1 wherein the mutant sequence is at least 97% identical to SEQ ID NO:2 or 4.

46 (new). The process of claim 1 wherein the mutant sequence is at least 98% identical to SEQ ID NO:2 or 4.

47 (new). The process of claim 1 wherein the mutant sequence is at least 99% identical to SEQ ID NO:2 or 4.

48 (new). The process of claim 1 wherein the polypeptide comprises SEQ ID NOs:2 or 4.

49 (new). The process of claim 1 wherein the produced arylsulfatase A consists of SEQ ID NO:3.

50 (new). The process of claim 1 wherein the nucleotide

sequence encodes a polypeptide consisting of (a) SEQ ID NOs:2 or 4 or (b) a mutant sequence at least 95% identical to SEQ ID NOs:2 or 4, and wherein said polypeptide, or a post-translationally modified product thereof that is produced by said cell, has arylsulfatase A activity.

51 (new). The process of claim 1 wherein the encoded polypeptide, when aligned by sequence alignment software to SEQ ID NO:2 or 4, has a cysteine in the position aligned with Cys-69 in SEQ ID NO: 2 or Cys-51 in SEQ ID NO:4.

52 (new). The process of claim 51 wherein a linear sequence of five amino acids within said polypeptide, and including said cysteine, is identical to the aligned sequence of five amino acids in SEQ ID NO:2 or SEQ ID NO:4.

53 (new). The process of claim 51 wherein a linear sequence of nine amino acids within said polypeptide, and including said cysteine, is identical to the aligned sequence of nine amino acids in SEQ ID NO:2 or SEQ ID NO:4.

54 (new). The process of claim 51 wherein a linear sequence of twenty amino acids within said polypeptide, and including said cysteine, is at least 95% identical to the aligned sequence of twenty amino acids in SEQ ID NO:2 or SEQ ID NO:4.

55 (new). The process of claim 51 wherein a linear sequence of twenty amino acids within said polypeptide, and including said cysteine, is identical to the aligned sequence of twenty amino acids in SEQ ID NO:2 or SEQ ID NO:4.

56 (New). The process of claim 51 wherein the encoded polypeptide comprises at least one putative N-glycosylation site.

57 (New). The process of claim 51 wherein at least putative N-glycosylation site is phosphorylable.

58 (New). The process of claim 51 wherein the encoded polypeptide, when aligned by sequence alignment software to SEQ ID NO:2 or 4, has asparagine in the positions aligned with Asn-158 and Asn=350 in SEQ ID NO: 2 or Asn-140 and Asn-332 in SEQ ID NO:4.

59 (New). The process of claim 58 wherein the encoded

polypeptide, when aligned by sequence alignment software to SEQ ID NO:2 or 4, has asparagine in the position aligned with Asn-184 in SEQ ID NO: 2 or Asn-166 in SEQ ID NO:4.